```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  Jul 12   BEILSTEIN enhanced with new display and select options,
                   resulting in a closer connection to BABS
 NEWS  4  Jul 30   BEILSTEIN on STN workshop to be held August 24 in conjunction
                   with the 228th ACS National Meeting
 NEWS  5  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                   fields
 NEWS  6  AUG 02   CAplus and CA patent records enhanced with European and Japan
                   Patent Office Classifications
 NEWS  7  AUG 02   The Analysis Edition of STN Express with Discover!
                   (Version 7.01 for Windows) now available
 NEWS  8  AUG 04   Pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover! will change September 1, 2004
 NEWS  9  AUG 27   BIOCOMMERCE: Changes and enhancements to content coverage
 NEWS 10  AUG 27   BIOTECHABS/BIOTECHDS: Two new display fields added for legal
                   status data from INPADOC
 NEWS 11  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS 12  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS 13  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS 14  SEP 14   STN Patent Forum to be held October 13, 2004, in Iselin, NJ

 NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:37:22 ON 23 SEP 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.
```

h eb c g cg b cg eb

STRUCTURE FILE UPDATES: 22 SEP 2004 HIGHEST RN 749824-02-0
DICTIONARY FILE UPDATES: 22 SEP 2004 HIGHEST RN 749824-02-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

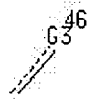
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

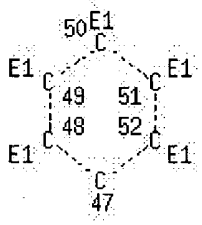
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

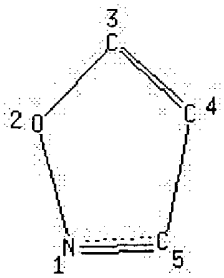
=>
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



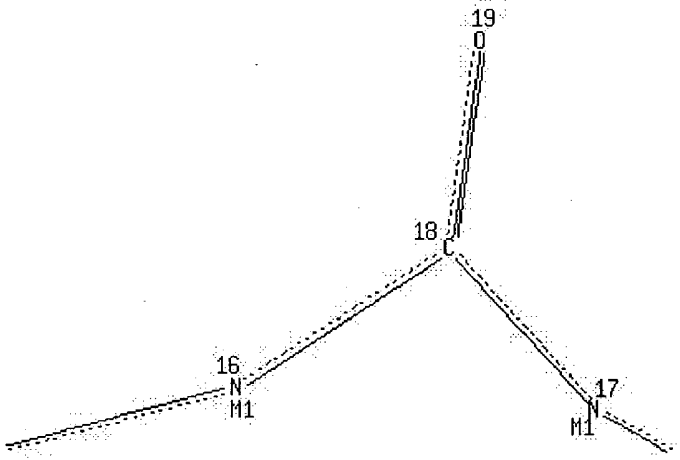
Page 1-B



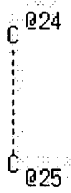


Page 1-D

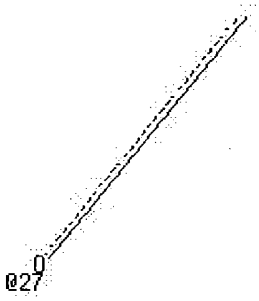
h eb c g cg b cg eb



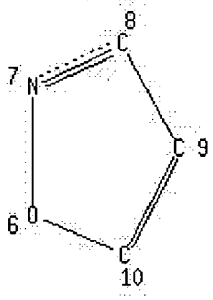
Page 1-E

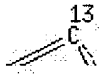


Page 2-A

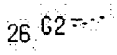


Page 2-B



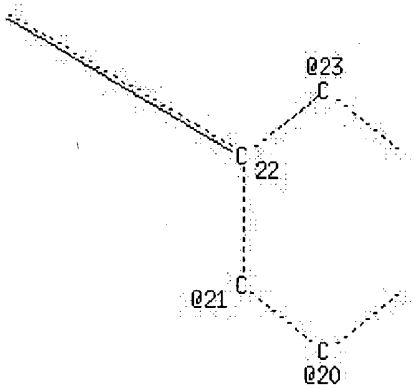


Page 2-D

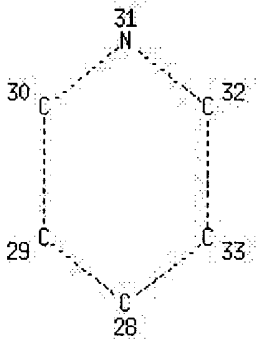


Page 2-E

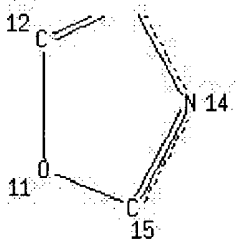
h eb c g cg b cg eb



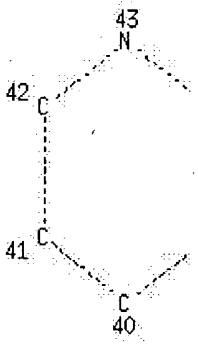
Page 2-F



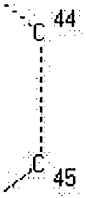
Page 3-B



Page 3-D

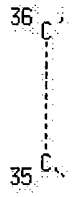


Page 3-E

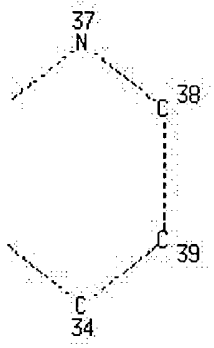


Page 3-F

h eb c g cg b cg eb



Page 4-E



Page 4-F
VAR G2=5/10/15
VAR G3=47/34/44
VPA 27-20/21/23/24/25 S
NODE ATTRIBUTES:

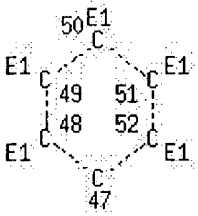
HCOUNT	IS M1	AT	16
HCOUNT	IS M1	AT	17
HCOUNT	IS E1	AT	48
HCOUNT	IS E1	AT	49
HCOUNT	IS E1	AT	50
HCOUNT	IS E1	AT	51
HCOUNT	IS E1	AT	52
NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS R	AT	6
NSPEC	IS R	AT	7
NSPEC	IS R	AT	8
NSPEC	IS R	AT	9
NSPEC	IS R	AT	10
NSPEC	IS R	AT	11
NSPEC	IS R	AT	12
NSPEC	IS R	AT	13
NSPEC	IS R	AT	14
NSPEC	IS R	AT	15
NSPEC	IS C	AT	16
NSPEC	IS C	AT	17
NSPEC	IS C	AT	18
NSPEC	IS C	AT	19
NSPEC	IS R	AT	20
NSPEC	IS R	AT	21
NSPEC	IS R	AT	22
NSPEC	IS R	AT	23
NSPEC	IS R	AT	24
NSPEC	IS R	AT	25
NSPEC	IS C	AT	26
NSPEC	IS C	AT	27
NSPEC	IS R	AT	28
NSPEC	IS R	AT	29

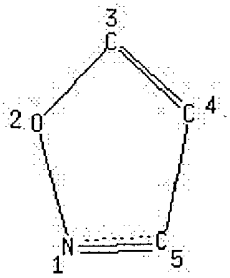
h eb c g cg b cg eb

```
NSPEC   IS R      AT  30
NSPEC   IS R      AT  31
NSPEC   IS R      AT  32
NSPEC   IS R      AT  33
NSPEC   IS R      AT  34
NSPEC   IS R      AT  35
NSPEC   IS R      AT  36
NSPEC   IS R      AT  37
NSPEC   IS R      AT  38
NSPEC   IS R      AT  39
NSPEC   IS R      AT  40
NSPEC   IS R      AT  41
NSPEC   IS R      AT  42
NSPEC   IS R      AT  43
NSPEC   IS R      AT  44
NSPEC   IS R      AT  45
NSPEC   IS C      AT  46
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  16 17 18 19 27 47 48 49 50 51 52
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  52

STEREO ATTRIBUTES: NONE


=> s l1
SAMPLE SEARCH INITIATED 13:47:16 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:47:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      6 TO ITERATE

100.0% PROCESSED       6 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L3            0 SEA SSS FUL L1

=>
L4      STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4              STR
```

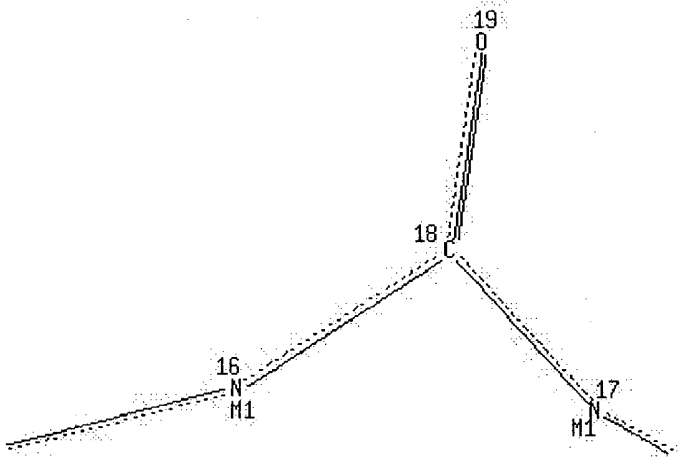
h eb c g cg b cg eb

Page 1-B

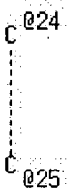




Page 1-D

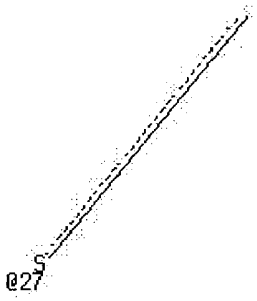


Page 1-E

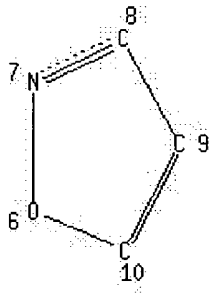


Page 2-A

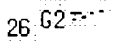
h eb c g cg b cg eb

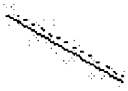


Page 2-B

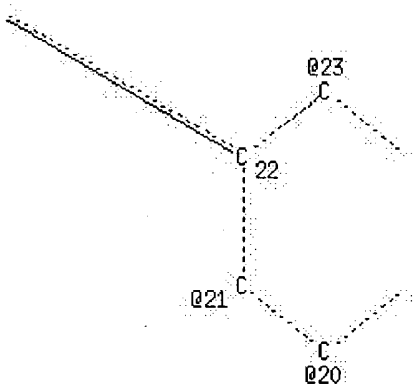


Page 2-D



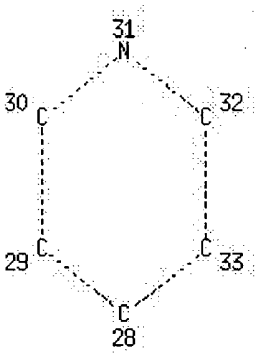


Page 2-E

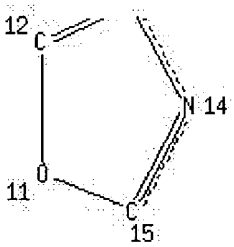


Page 2-F

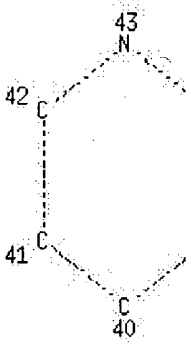
h eb c g cg b cg eb



Page 3-B



Page 3-D

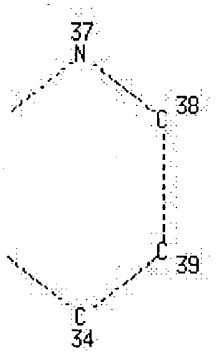


Page 3-E

Page 3-F

Page 4-E

h eb c g cg b cg eb




```
Page 4-F
VAR G2=5/10/15
VAR G3=47/34/44
VPA 27-20/21/23/24/25 S
NODE ATTRIBUTES:
HCOUNT  IS M1     AT  16
HCOUNT  IS M1     AT  17
HCOUNT  IS E1     AT  48
HCOUNT  IS E1     AT  49
HCOUNT  IS E1     AT  50
HCOUNT  IS E1     AT  51
HCOUNT  IS E1     AT  52
NSPEC   IS R      AT   1
NSPEC   IS R      AT   2
NSPEC   IS R      AT   3
NSPEC   IS R      AT   4
NSPEC   IS R      AT   5
NSPEC   IS R      AT   6
NSPEC   IS R      AT   7
NSPEC   IS R      AT   8
NSPEC   IS R      AT   9
NSPEC   IS R      AT  10
NSPEC   IS R      AT  11
NSPEC   IS R      AT  12
NSPEC   IS R      AT  13
NSPEC   IS R      AT  14
NSPEC   IS R      AT  15
NSPEC   IS C      AT  16
NSPEC   IS C      AT  17
NSPEC   IS C      AT  18
NSPEC   IS C      AT  19
NSPEC   IS R      AT  20
NSPEC   IS R      AT  21
NSPEC   IS R      AT  22
NSPEC   IS R      AT  23
NSPEC   IS R      AT  24
NSPEC   IS R      AT  25
NSPEC   IS C      AT  26
NSPEC   IS C      AT  27
NSPEC   IS R      AT  28
NSPEC   IS R      AT  29
NSPEC   IS R      AT  30
NSPEC   IS R      AT  31
NSPEC   IS R      AT  32
NSPEC   IS R      AT  33
NSPEC   IS R      AT  34
NSPEC   IS R      AT  35
NSPEC   IS R      AT  36
```

h eb c g cg b cg eb

```
NSPEC   IS R      AT  37
NSPEC   IS R      AT  38
NSPEC   IS R      AT  39
NSPEC   IS R      AT  40
NSPEC   IS R      AT  41
NSPEC   IS R      AT  42
NSPEC   IS R      AT  43
NSPEC   IS R      AT  44
NSPEC   IS R      AT  45
NSPEC   IS C      AT  46
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  16 17 18 19 27 47 48 49 50 51 52
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  52

STEREO ATTRIBUTES: NONE


=> s l4
SAMPLE SEARCH INITIATED 13:47:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L5            0 SEA SSS SAM L4

=> s l4 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:48:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L6            0 SEA SSS FUL L4

=>
L7      STRUCTURE UPLOADED

=>  l7
L7 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l7
L7 HAS NO ANSWERS
L7              STR

=> s l7
```

h eb c g cg b cg eb

```
SAMPLE SEARCH INITIATED 13:52:02 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     60 TO ITERATE

100.0% PROCESSED      60 ITERATIONS                              23 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          736 TO     1664
PROJECTED ANSWERS:             173 TO      747

L8           23 SEA SSS SAM L7

=>
L9       STRUCTURE UPLOADED

=> s l9
SAMPLE SEARCH INITIATED 13:58:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      8 TO ITERATE

100.0% PROCESSED       8 ITERATIONS                               6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            8 TO      329
PROJECTED ANSWERS:               6 TO      266

L10           6 SEA SSS SAM L9

=> s l9 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:58:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    185 TO ITERATE

100.0% PROCESSED     185 ITERATIONS                             135 ANSWERS
SEARCH TIME: 00.00.01

L11          135 SEA SSS FUL L9

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               480.12     480.33

FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
```

h eb c g cg b cg eb

FILE COVERS 1907 - 23 Sep 2004 VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004 (20040922/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l11
L12 5 L11

=> s l12 and dumas, j?/au
677 DUMAS, J?/AU
L13 3 L12 AND DUMAS, J?/AU

=> d l13, ibib abs fhitstr, 1-3

L13 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

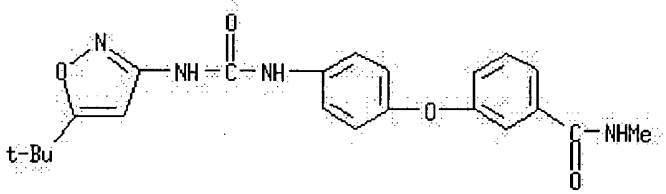
Full Text | Other Sources | References

ACCESSION NUMBER: 2004:51821 HCAPLUS
DOCUMENT NUMBER: 140:296858
TITLE: Omega-carboxypyridyl substituted ureas as Raf kinase inhibitors: SAR of the amide substituent
AUTHOR(S): Khire, Uday R.; Bankston, Donald; Barbosa, James; Brittelli, David R.; Caringal, Yolanda; Carlson, Robert; **Dumas, Jacques**; Gane, Todd; Heald, Sarah L.; Hibner, Barbara; Johnson, Jeffrey S.; Katz, Michael E.; Kennure, Nancy; Kingery-Wood, Jill; Lee, Wendy; Liu, Xiao-Gao; Lowinger, Timothy B.; McAlexander, Ian; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Riedl, Bernd; Rong, Hong; Sibley, Robert N.; Smith, Roger A.; Wolanin, Donald
CORPORATE SOURCE: Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 783-786
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bis-aryl ureas have been disclosed previously as a potent class of Raf kinase inhibitors. Modifications in the amide portion led to an improvement in aq. soly., an important characteristic for an oral drug. Based on this finding, we hypothesize that this portion of the mol. is directed towards the solvent in Raf-1.

IT **228999-58-4**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(structure and Raf kinase inhibitor activity of amide substituent of omega-carboxypyridyl substituted ureas)
RN 228999-58-4 HCAPLUS
CN Benzamide, 3-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

h eb c g cg b cg eb



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

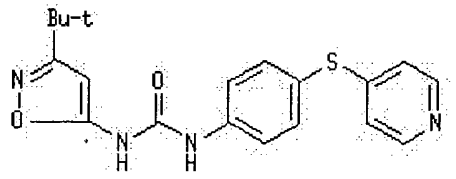
L13 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425745 HCAPLUS
DOCUMENT NUMBER: 131:87909
TITLE: Inhibition of p38 kinase activity using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932111	A1	19990701	WO 1998-US26080	19981222
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315720	AA	19990701	CA 1998-2315720	19981222
AU 9919971	A1	19990712	AU 1999-19971	19981222
AU 739642	B2	20011018		
EP 1041982	A1	20001011	EP 1998-964709	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001526223	T2	20011218	JP 2000-525102	19981222
PRIORITY APPLN. INFO.:			US 1997-995750 A	19971222
			WO 1998-US26080 W	19981222

OTHER SOURCE(S): MARPAT 131:87909
GI



II

AB A method for treatment of p38-mediated disease other than cancer comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 kinase assay, I displayed IC50 values of 1-10 μM.

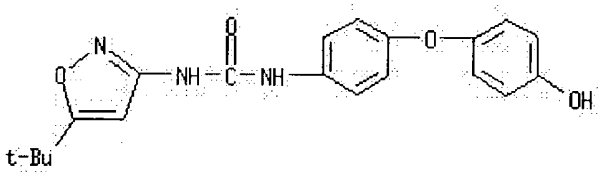
IT **228999-08-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than cancer)

RN 228999-08-4 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425740 HCAPLUS
DOCUMENT NUMBER: 131:73648
TITLE: Inhibition of raf kinase using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932106	A1	19990701	WO 1998-US26078	19981222

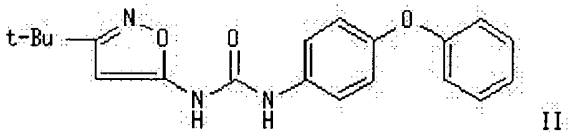
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,

h eb c g cg b cg eb

KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2315717	AA	19990701	CA 1998-2315717	19981222
AU 9921989	A1	19990712	AU 1999-21989	19981222
EP 1047418	A1	20001102	EP 1998-965981	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002618	T2	20010420	TR 2000-200002618	19981222
JP 2001526220	T2	20011218	JP 2000-525097	19981222
BR 9814374	A	20020514	BR 1998-14374	19981222
RU 2232015	C2	20040710	RU 2000-120184	19981222
NO 2000003232	A	20000821	NO 2000-3232	20000621
BG 104597	A	20010228	BG 2000-104597	20000712
PRIORITY APPLN. INFO.:			US 1997-996343 A	19971222
			WO 1998-US26078 W	19981222

OTHER SOURCE(S): MARPAT 131:73648
GI

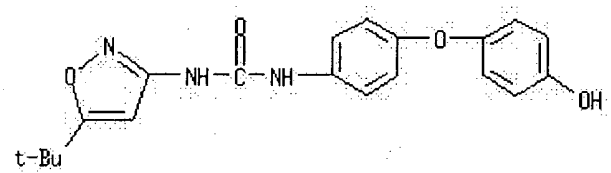


II

AB A method for treatment of cancerous cell growth mediated by raf kinase comprises administration of urea derivs. ANHCONHB [I; A = substituted isoxazolyl, thienyl, thiadiazolyl, furyl, pyrazolyl, etc.; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-phenyloxyphenyl isocyanate with 5-amino-3-tert-butylisoxazole in methylene chloride and heating at reflux temp. for 2 days gave title compd. II. In an in vitro raf kinase assay, I displayed IC50 values of 1-10 μM.

IT **228999-08-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by raf kinase)

RN 228999-08-4 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

h eb c g cg b cg eb

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d his

     (FILE 'HOME' ENTERED AT 13:37:22 ON 23 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           0 S L1 FULL
L4             STRUCTURE UPLOADED
L5           0 S L4
L6           0 S L4 FULL
L7             STRUCTURE UPLOADED
L8          23 S L7
L9             STRUCTURE UPLOADED
L10          6 S L9
L11        135 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
L12          5 S L11
L13          3 S L12 AND DUMAS, J?/AU

=> s l12 not l13
L14          2 L12 NOT L13

=> s l14 and khire, u?/au
            41 KHIRE, U?/AU
L15          0 L14 AND KHIRE, U?/AU

=> s l12 and lowinger, t?/au
            44 LOWINGER, T?/AU
L16          4 L12 AND LOWINGER, T?/AU

=> s l16 not l13
L17          1 L16 NOT L13

=> d l17,  ibib abs fhitstr, 1

L17  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Other References

ACCESSION NUMBER: 2001:746592 HCAPLUS
DOCUMENT NUMBER: 136:95577
TITLE: Discovery of heterocyclic ureas as a new class of raf kinase inhibitors: identification of a second generation lead by a combinatorial chemistry approach
AUTHOR(S): Smith, R. A.; Barbosa, J.; Blum, C. L.; Bobko, M. A.; Caringal, Y. V.; Dally, R.; Johnson, J. S.; Katz, M. E.; Kennure, N.; Kingery-Wood, J.; Lee, W.; **Lowinger, T. B.**; Lyons, J.; Marsh, V.; Rogers, D. H.; Swartz, S.; Walling, T.; Wild, H.
CORPORATE SOURCE: Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(20), 2775-2778
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

h eb c g cg b cg eb

LANGUAGE: English

AB Heterocyclic ureas, such as N-3-thienyl N'-aryl ureas, have been identified as novel inhibitors of raf kinase, a key mediator in the ras signal transduction pathway. Structure-activity relationships were established, and the potency of the screening hit was improved 10-fold to IC50=1.7 μM. A combinatorial synthesis approach enabled the identification of a breakthrough lead (IC50=0.54 μM) for a second generation series of heterocyclic urea raf kinase inhibitors.

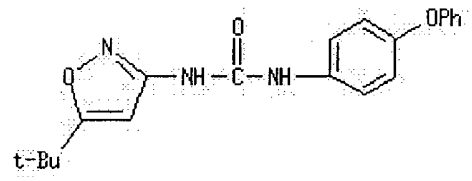
IT **228998-90-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(heterocyclic ureas as raf kinase inhibitors)

RN 228998-90-1 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	26.12	506.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.80	-2.80

FILE 'CAOLD' ENTERED AT 14:00:44 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGistRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d his

(FILE 'HOME' ENTERED AT 13:37:22 ON 23 SEP 2004)

h eb c g cg b cg eb

```
     FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
L1                STRUCTURE UPLOADED
L2              0 S L1
L3              0 S L1 FULL
L4                STRUCTURE UPLOADED
L5              0 S L4
L6              0 S L4 FULL
L7                STRUCTURE UPLOADED
L8             23 S L7
L9                STRUCTURE UPLOADED
L10             6 S L9
L11           135 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
L12             5 S L11
L13             3 S L12 AND DUMAS, J?/AU
L14             2 S L12 NOT L13
L15             0 S L14 AND KHIRE, U?/AU
L16             4 S L12 AND LOWINGER, T?/AU
L17             1 S L16 NOT L13

     FILE 'CAOLD' ENTERED AT 14:00:44 ON 23 SEP 2004

=> s l11
L18           0 L11

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.42     506.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -2.80

FILE 'REGISTRY' ENTERED AT 14:00:55 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   22 SEP 2004  HIGHEST RN 749824-02-0
DICTIONARY FILE UPDATES:  22 SEP 2004  HIGHEST RN 749824-02-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
```

h eb c g cg b cg eb

```
L19     STRUCTURE UPLOADED

=> d l19
L19 HAS NO ANSWERS
L19             STR

=> s l19
SAMPLE SEARCH INITIATED 14:13:16 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L20           0 SEA SSS SAM L19

=> s l19 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 14:13:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     40 TO ITERATE

100.0% PROCESSED      40 ITERATIONS                               32 ANSWERS
SEARCH TIME: 00.00.01

L21          32 SEA SSS FUL L19

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              163.82     670.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                                0.00      -2.80

FILE 'HCAPLUS' ENTERED AT 14:13:24 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 23 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 22 Sep 2004  (20040922/ED)

 This file contains CAS Registry Numbers for easy and accurate
```

h eb c g cg b cg eb

substance identification.

```
=> s l21
L22           4 L21

=> s l22 and dumas, j?/au
            677 DUMAS, J?/AU
L23           2 L22 AND DUMAS, J?/AU

=> d l23, ibib abs fhitstr, 1-2

L23  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

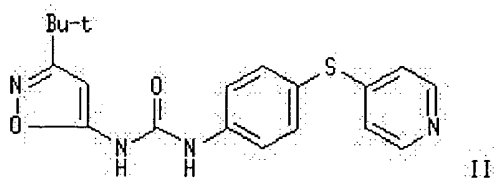
Full Text | Other References

ACCESSION NUMBER: 1999:425745 HCAPLUS
DOCUMENT NUMBER: 131:87909
TITLE: Inhibition of p38 kinase activity using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932111	A1	19990701	WO 1998-US26080	19981222
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315720	AA	19990701	CA 1998-2315720	19981222
AU 9919971	A1	19990712	AU 1999-19971	19981222
AU 739642	B2	20011018		
EP 1041982	A1	20001011	EP 1998-964709	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001526223	T2	20011218	JP 2000-525102	19981222
PRIORITY APPLN. INFO.:			US 1997-995750 A	19971222
			WO 1998-US26080 W	19981222

OTHER SOURCE(S): MARPAT 131:87909
GI

h eb c g cg b cg eb



II

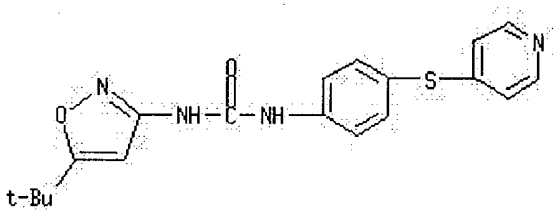
AB A method for treatment of p38-mediated disease other than cancer comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 kinase assay, I displayed IC50 values of 1-10 μM.

IT **228999-10-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than cancer)

RN 228999-10-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-pyridinylthio)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425740 HCAPLUS

DOCUMENT NUMBER: 131:73648

TITLE: Inhibition of raf kinase using substituted heterocyclic ureas

INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932106	A1	19990701	WO 1998-US26078	19981222

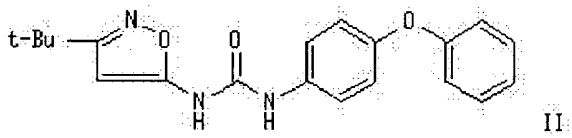
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,

h eb c g cg b cg eb

KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2315717	AA	19990701	CA 1998-2315717		19981222
AU 9921989	A1	19990712	AU 1999-21989		19981222
EP 1047418	A1	20001102	EP 1998-965981		19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
TR 200002618	T2	20010420	TR 2000-200002618		19981222
JP 2001526220	T2	20011218	JP 2000-525097		19981222
BR 9814374	A	20020514	BR 1998-14374		19981222
RU 2232015	C2	20040710	RU 2000-120184		19981222
NO 2000003232	A	20000821	NO 2000-3232		20000621
BG 104597	A	20010228	BG 2000-104597		20000712
PRIORITY APPLN. INFO.:			US 1997-996343	A	19971222
			WO 1998-US26078	W	19981222

OTHER SOURCE(S): MARPAT 131:73648
GI

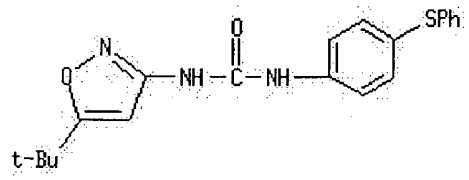


II

AB A method for treatment of cancerous cell growth mediated by raf kinase comprises administration of urea derivs. ANHCONHB [I; A = substituted isoxazolyl, thienyl, thiadiazolyl, furyl, pyrazolyl, etc.; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-phenyloxyphenyl isocyanate with 5-amino-3-tert-butylisoxazole in methylene chloride and heating at reflux temp. for 2 days gave title compd. II. In an in vitro raf kinase assay, I displayed IC50 values of 1-10 μM.

IT **228998-97-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by raf kinase)

RN 228998-97-8 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(phenylthio)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

h eb c g cg b cg eb

```
=> d his

     (FILE 'HOME' ENTERED AT 13:37:22 ON 23 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           0 S L1 FULL
L4             STRUCTURE UPLOADED
L5           0 S L4
L6           0 S L4 FULL
L7             STRUCTURE UPLOADED
L8          23 S L7
L9             STRUCTURE UPLOADED
L10          6 S L9
L11        135 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
L12          5 S L11
L13          3 S L12 AND DUMAS, J?/AU
L14          2 S L12 NOT L13
L15          0 S L14 AND KHIRE, U?/AU
L16          4 S L12 AND LOWINGER, T?/AU
L17          1 S L16 NOT L13

     FILE 'CAOLD' ENTERED AT 14:00:44 ON 23 SEP 2004
L18          0 S L11

     FILE 'REGISTRY' ENTERED AT 14:00:55 ON 23 SEP 2004
L19            STRUCTURE UPLOADED
L20          0 S L19
L21         32 S L19 FULL

     FILE 'HCAPLUS' ENTERED AT 14:13:24 ON 23 SEP 2004
L22          4 S L21
L23          2 S L22 AND DUMAS, J?/AU

=> s l22 not l23
L24          2 L22 NOT L23

=> s l24 and khire, u?/au
            41 KHIRE, U?/AU
L25          0 L24 AND KHIRE, U?/AU

=> s l24 and lowinger, t?/au
            44 LOWINGER, T?/AU
L26          0 L24 AND LOWINGER, T?/AU

=> s l24 and riedl, b?/au
           167 RIEDL, B?/AU
L27          0 L24 AND RIEDL, B?/AU

=> s l24 and scott, w?/au
          1980 SCOTT, W?/AU
L28          0 L24 AND SCOTT, W?/AU

=> s l24 and smith, r?/au
         13627 SMITH, R?/AU
```

h eb c g cg b cg eb

```
L29             0 L24 AND SMITH, R?/AU

=> s 124 and wood, j?/au
          3937 WOOD, J?/AU
L30             0 L24 AND WOOD, J?/AU

=> s 124 and hatoum-mokdad, h?/au
            27 HATOUM-MOKDAD, H?/AU
L31             0 L24 AND HATOUM-MOKDAD, H?/AU

=> s 124 and johnson, j?/au
          7804 JOHNSON, J?/AU
L32             0 L24 AND JOHNSON, J?/AU

=> s 124 and lee, w?/au
          8978 LEE, W?/AU
L33             0 L24 AND LEE, W?/AU

=> s 124 and redman, a?/au
            33 REDMAN, A?/AU
L34             0 L24 AND REDMAN, A?/AU

=> s 124 and sibley, r?/au
           193 SIBLEY, R?/AU
L35             0 L24 AND SIBLEY, R?/AU

=> s 124 and renick, j?/au
            14 RENICK, J?/AU
L36             0 L24 AND RENICK, J?/AU

=> d his

     (FILE 'HOME' ENTERED AT 13:37:22 ON 23 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
L1                STRUCTURE UPLOADED
L2              0 S L1
L3              0 S L1 FULL
L4                STRUCTURE UPLOADED
L5              0 S L4
L6              0 S L4 FULL
L7                STRUCTURE UPLOADED
L8             23 S L7
L9                STRUCTURE UPLOADED
L10             6 S L9
L11           135 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
L12             5 S L11
L13             3 S L12 AND DUMAS, J?/AU
L14             2 S L12 NOT L13
L15             0 S L14 AND KHIRE, U?/AU
L16             4 S L12 AND LOWINGER, T?/AU
L17             1 S L16 NOT L13

     FILE 'CAOLD' ENTERED AT 14:00:44 ON 23 SEP 2004
L18             0 S L11

     FILE 'REGISTRY' ENTERED AT 14:00:55 ON 23 SEP 2004
L19               STRUCTURE UPLOADED
```

h ebc gcg b cg eb

```
L20             0 S L19
L21            32 S L19 FULL

     FILE 'HCAPLUS' ENTERED AT 14:13:24 ON 23 SEP 2004
L22             4 S L21
L23             2 S L22 AND DUMAS, J?/AU
L24             2 S L22 NOT L23
L25             0 S L24 AND KHIRE, U?/AU
L26             0 S L24 AND LOWINGER, T?/AU
L27             0 S L24 AND RIEDL, B?/AU
L28             0 S L24 AND SCOTT, W?/AU
L29             0 S L24 AND SMITH, R?/AU
L30             0 S L24 AND WOOD, J?/AU
L31             0 S L24 AND HATOUM-MOKDAD, H?/AU
L32             0 S L24 AND JOHNSON, J?/AU
L33             0 S L24 AND LEE, W?/AU
L34             0 S L24 AND REDMAN, A?/AU
L35             0 S L24 AND SIBLEY, R?/AU
L36             0 S L24 AND RENICK, J?/AU

=> d l24, ibib abs fhitstr, 1-2

L24  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:          2002:107924  HCAPLUS
DOCUMENT NUMBER:           136:167692
TITLE:                     Preparation of new biphenyl and biphenyl-analogous
                           compounds as integrin antagonists
INVENTOR(S):               Albers, Markus; Urbahns, Klaus; Vaupel, Andrea;
                           Harter, Michael; Schmidt, Delf; Stelte-Ludwig,
                           Beatrix; Gerdes, Christoph; Stahl, Elke; Keldenich,
                           Jorg; Brueggemeier, Ulf; Lustig, Klemens
PATENT ASSIGNEE(S):        Bayer Aktiengesellschaft, Germany
SOURCE:                    U.S. Pat. Appl. Publ., 256 pp., Division of U.S. Ser.
                           No. 464,237.
                           CODEN: USXXCO
DOCUMENT TYPE:             Patent
LANGUAGE:                  English
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
     ----------            ----   --------    ---------------------    --------
     US 2002016461         A1     20020207    US 2001-828514           20010406
     US 6677360            B2     20040113
     US 6420396            B1     20020716    US 1999-464237           19991215
     US 2004030132         A1     20040212    US 2002-285073           20021031
PRIORITY APPLN. INFO.:                         US 1998-172225P     P    19981216
                                               US 1999-464237      A3   19991215
                                               US 1999-172217P     P    19991019
                                               US 2001-828514      A3   20010406
OTHER SOURCE(S):           MARPAT 136:167692
AB   Biphenylyl compds. R1O2CCHR2-U-V-A-B-W-NR3-C-R4 [R1 = H, (un)substituted
     alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl; R2 = H,
     (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl,
     alkenyl, alkynyl, -NR2'SO2R2'', -NR2'CO2R2', -NR2'COR2', -NR2'CONR2'2,
     -NR2'CSNR2'2 (R2' has same definition as R1 and R2'' has same definition
     as R1 except it is not H); U or W is a direct bond or (un)substituted
     alkylene; V = (un)substituted alkylene, -NR2'CO- or NR2'SO2-; A and B =
```

h eb c g cg b cg eb

(un)substituted 1,3- or 1,4-bridging phenylene group or a 2,4- or 2,5-bridging thienylene group, each of which may have substituents; C is a direct bond, CMe(:X-R5)-Y-N(R6)- (R5 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, acyl, carboxylic or carboxylate group or is connected to R3, Y, R4 or R6, if present; R6 is H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R3, R4, Y, or R5, if present, to form a heterocyclic ring system; X = CHNO2, CHCN, O, N or S; Y is a direct bond or (un)substituted alkylene or alkyne group) or 3,4-dioxo-1,2-cyclobutenediyl-NR6-; R3, R4 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R4 (or R3), Y, R5 or R6, if present, to form a heterocyclic ring system] were prepd. as integrin antagonists. For example, (2R,S)-3-[3-(pyridin-3-ylmethylureido)biphenyl-4-yl]-2-[2,4,6-trimethylbenzenesulfonylamino]propanoic acid, prepd. by reactions of resin-bound (2R,S)-3-(4-bromophenyl)-2-(9-fluorenylmethoxycarbonylamino)propanoic acid with sulfonylating, boronic acid, and amine reagents (mesitylenesulfonyl chloride, 3-nitrobenzeneboronic acid, and 2-aminomethylpyridine), showed IC50 = 5 nM for binding to the αvβ3 receptor and IC50 = 480 nM in the smooth muscle cell migration test. Thus, the invention compds. are useful for the inhibition of angiogenesis and/or for therapy and prophylaxis of cancer, osteolytic diseases such as osteoporosis, arteriosclerosis, restenosis, rheumatoid arthritis, and ophthalmic disorders (no data).

IT **276261-89-3P**

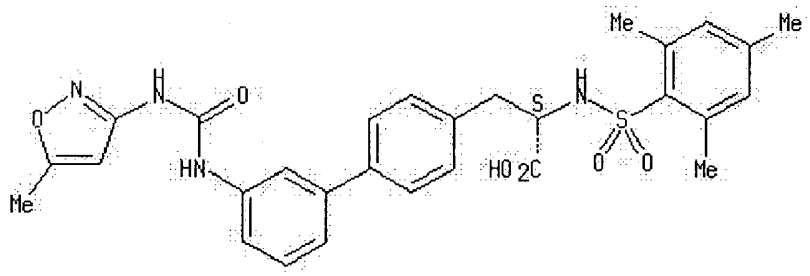
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of biphenyl amino acid analogs as integrin antagonists for inhibition of angiogenesis and treatment of cancer, osteolytic diseases, arteriosclerosis, restenosis, rheumatoid arthritis, and ophthalmic disorders)

RN 276261-89-3 HCAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 3'-[[[(5-methyl-3-isoxazolyl)amino]carbonyl]amino]-α-[[(2,4,6-trimethylphenyl)sulfonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:421093 HCAPLUS

DOCUMENT NUMBER: 133:43809

TITLE: Preparation of new biphenyl and biphenyl-analogous compounds as integrin antagonists

INVENTOR(S): Albers, Markus; Urbahns, Klaus; Vaupel, Andrea; Harter, Michael; Schmidt, Delf; Stelte-ludwig, Beatrix; Gerdes, Christoph; Stahl, Elke; Keldenich,

h eb c g cg b cg eb

Jorg; Bruggemeier, Ulf; Lustig, Klemens
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany; et al.
SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035864	A1	20000622	WO 1999-EP9843	19991213
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140809	A1	20011010	EP 1999-967934	19991213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916367	A	20011030	BR 1999-16367	19991213
TR 200102498	T2	20020221	TR 2001-200102498	19991213
EE 200100317	A	20020815	EE 2001-317	19991213
JP 2002532465	T2	20021002	JP 2000-588126	19991213
NZ 512339	A	20030328	NZ 1999-512339	19991213
AU 761407	B2	20030605	AU 2000-24312	19991213
ZA 2001014432	A	20020530	ZA 2001-14432	20010530
BG 105574	A	20020131	BG 2001-105574	20010607
NO 2001002975	A	20010813	NO 2001-2975	20010615
HR 2001000531	A1	20020831	HR 2001-531	20010716
PRIORITY APPLN. INFO.:			US 1998-213381 A	19981216
			WO 1999-EP9843 W	19991213

OTHER SOURCE(S): MARPAT 133:43809

AB Biphenylyl compds. R1O2CCHR2-U-V-A-B-W-NR3-C-R4 [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl; R2 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, alkenyl, alkynyl, -NR2'SO2R2'', -NR2'CO2R2', -NR2'COR2', -NR2'CONR2'2, -NR2'CSNR2'2 (R2' has same definition as R1 and R2'' has same definition as R1 except it is not H); U or W is a direct bond or (un)substituted alkylene; V = (un)substituted alkylene, -NR2'CO- or NR2'SO2-; A and B = (un)substituted 1,3- or 1,4-bridging phenylene group or a 2,4- or 2,5-bridging thienylene group, each of which may have substituents; C is a direct bond, CMe(:X-R5)-Y-N(R6)- (R5 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, acyl, carboxylic or carboxylate group or is connected to R3, Y, R4 or R6, if present; R6 is H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R3, R4, Y, or R5, if present, to form a heterocyclic ring system; X = CHNO2, CHCN, O, N or S; Y is a direct bond or (un)substituted alkylene or alkyne group) or 3,4-dioxo-1,2-cyclobutenediyl-NR6-; R3, R4 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R4 (or R3), Y, R5 or R6, if present, to form a heterocyclic ring system] were prepd. as integrin antagonists. Thus, (2R,S)-3-[3-(pyridin-3-ylmethylureido)biphenyl-4-yl]-2-[2,4,6-trimethylbenzenesulfonylamino]propanoic acid, prepd. by reactions of resin-bound (2R,S)-3-(4-bromophenyl)-2-(9-fluorenylmethoxycarbonylamino)pr

h eb c g cg b cg eb

opanoic acid with sulfonylating, boronic acid, and amine reagents (mesitylenesulfonyl chloride, 3-nitrobenzeneboronic acid, and 2-aminomethylpyridine), showed IC50 = 5 nM for binding to the αvβ3 receptor and IC50 = 480 nM in the smooth muscle cell migration test.

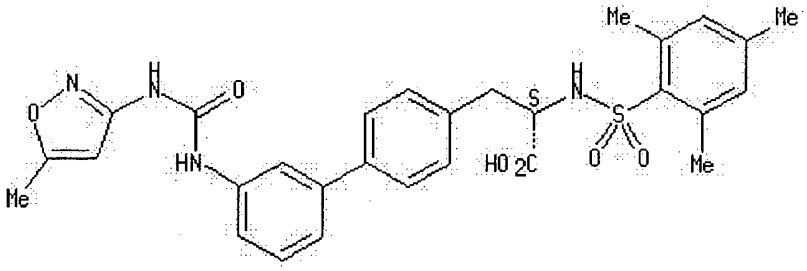
IT **276261-89-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

RN 276261-89-3 HCAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 3'-[[[(5-methyl-3-isoxazolyl)amino]carbonyl]amino]-α-[[(2,4,6-trimethylphenyl)sulfonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	26.12	696.81

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.80	-5.60

FILE 'CAOLD' ENTERED AT 14:15:26 ON 23 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

h eb c g cg b cg eb

```
=> d his

     (FILE 'HOME' ENTERED AT 13:37:22 ON 23 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 13:37:27 ON 23 SEP 2004
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           0 S L1 FULL
L4             STRUCTURE UPLOADED
L5           0 S L4
L6           0 S L4 FULL
L7             STRUCTURE UPLOADED
L8          23 S L7
L9             STRUCTURE UPLOADED
L10          6 S L9
L11        135 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 13:58:54 ON 23 SEP 2004
L12          5 S L11
L13          3 S L12 AND DUMAS, J?/AU
L14          2 S L12 NOT L13
L15          0 S L14 AND KHIRE, U?/AU
L16          4 S L12 AND LOWINGER, T?/AU
L17          1 S L16 NOT L13

     FILE 'CAOLD' ENTERED AT 14:00:44 ON 23 SEP 2004
L18          0 S L11

     FILE 'REGISTRY' ENTERED AT 14:00:55 ON 23 SEP 2004
L19            STRUCTURE UPLOADED
L20          0 S L19
L21         32 S L19 FULL

     FILE 'HCAPLUS' ENTERED AT 14:13:24 ON 23 SEP 2004
L22          4 S L21
L23          2 S L22 AND DUMAS, J?/AU
L24          2 S L22 NOT L23
L25          0 S L24 AND KHIRE, U?/AU
L26          0 S L24 AND LOWINGER, T?/AU
L27          0 S L24 AND RIEDL, B?/AU
L28          0 S L24 AND SCOTT, W?/AU
L29          0 S L24 AND SMITH, R?/AU
L30          0 S L24 AND WOOD, J?/AU
L31          0 S L24 AND HATOUM-MOKDAD, H?/AU
L32          0 S L24 AND JOHNSON, J?/AU
L33          0 S L24 AND LEE, W?/AU
L34          0 S L24 AND REDMAN, A?/AU
L35          0 S L24 AND SIBLEY, R?/AU
L36          0 S L24 AND RENICK, J?/AU

     FILE 'CAOLD' ENTERED AT 14:15:26 ON 23 SEP 2004

=> s l21
L37          0 L21

=> log y
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY     SESSION
FULL ESTIMATED COST                            0.42      697.23
```

h eb c g cg b cg eb

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-5.60

STN INTERNATIONAL LOGOFF AT 14:15:36 ON 23 SEP 2004

h eb c g cg b cg eb